

## **REMARKS**

Further and favorable reconsideration is respectfully requested in view of the foregoing amendments and following remarks.

### **Claim Amendments**

Claim 1 has been amended to limit the local anesthetic to lidocaine. Support for this amendment is found in original claim 4, and on page 8, line 23 of Applicants' specification. Claim 3 has been amended to be consistent with amended claim 1.

Claims 2 and 4-6 have been cancelled, without prejudice or disclaimer.

New claims 7 and 8 have been added. New claim 7 recites a molar ratio of lidocaine to etodolac, based upon page 10, lines 13 and 14 of Applicants' specification. New claim 8 recites a plaster preparation comprising the anti-inflammatory analgesic of claim 1, based upon page 11, line 2 of Applicants' specification.

### **Patentability Arguments**

The patentability of the present invention over the disclosure of the reference relied upon by the Examiner in rejecting the claims will be apparent upon consideration of the following remarks.

### **Rejection Under 35 U.S.C. § 103(a)**

Claims 1-6 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Lee et al. (U.S. Patent No. 7,166,641, hereafter "Lee").

This rejection is respectfully traversed for the reasons set forth below.

### **The Position of the Examiner**

The Examiner takes the position that Lee teaches a group of novel pharmaceutically acceptable salts, each containing local anesthetic and anti-inflammatory activities, wherein the preferred pharmaceutically acceptable salt is diclofenac salt of lidocaine. The Examiner states that other NSAIDS, such as etodolac, may be used to replace diclofenac. The Examiner asserts

that it would have been obvious to one of ordinary skill in the art at the time of the invention to have formulated the composition of NSAID with lidocaine as taught by Lee, and employed etodolac as the NSAID.

Applicants' Arguments

Applicants' independent claim 1 requires an anti-inflammatory analgesic for external use comprising etodolac and lidocaine. New claim 8 requires a plaster preparation comprising said anti-inflammatory analgesic.

According to the present application, the penetratability and diffusivity in muscle tissues are unexpectedly improved together with skin permeability of etodolac, by adding lidocaine. Please see page 9, lines 12-26 of Applicants' specification. Applicants have discovered that lidocaine works as a superior enhancer of the transdermal absorption of etodolac. Please see page 6, line 24 to page 7, line 1 of Applicants' specification.

On the contrary, Lee describes that a diclofenac salt of lidocaine is the preferred one in the various combinations of NSAID and a local anesthetic. Please see column 4, line 18 of the reference. Further, Lee describes that diclofenac is replaceable with another NSAID, and ketorolac is preferred among these other NSAIDS. Please see column 4, line 38 of the reference.

Contrary to the teachings of Lee, Applicants have discovered the specific combination of lidocaine and etodolac, which achieves unexpected results and superior results. Lee fails to teach or suggest this particular combination, or to recognize the superior effects resulting therefrom.

In order to support this assertion, Applicants have compared the enhancing effect of lidocaine on the transdermal absorption of etodolac with that of diclofenac or ketorolac. As shown in the enclosed Declaration of Mr. H. Hamamoto, the enhancing effect on etodolac-transdermal absorption is **far more potent** than the effect on diclofenac- or ketorolac-transdermal absorption.

One of ordinary skill in the art would not have expected such an unexpected and superior result from the combination of lidocaine and etodolac, based upon the teachings of Lee.

MPEP 716.02(a) states that "Evidence of unobvious or unexpected advantageous properties, **such as superiority in a property the claimed compound shares with the prior art**, can rebut *prima facie* obviousness. 'Evidence that a compound is unexpectedly superior in

one of a spectrum of common properties . . . can be enough to rebut a *prima facie* case of obviousness.”” (Emphasis added.)

Accordingly, Applicants respectfully assert that the claimed anti-inflammatory analgesic is patentable over the teachings of the cited art, due to the unexpected results discussed above. For these reasons, the invention of Applicants’ claims is clearly patentable over the teachings of Lee.

### Conclusion

Therefore, in view of the foregoing amendments and remarks, it is submitted that the ground of rejection set forth by the Examiner has been overcome, and that the application is in condition for allowance. Such allowance is solicited.

If, after reviewing this Amendment, the Examiner feels there are any issues remaining which must be resolved before the application can be passed to issue, the Examiner is respectfully requested to contact the undersigned by telephone in order to resolve such issues. Respectfully submitted,

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